THE IMPACT OF SONICATION CELL SIZE AND DISTANCE ON NEAR FIELD TEMPERATURE IN MAGNETIC RESONANCE GUIDED HIGH INTENSITY FOCUSED ULTRASOUND.

DR NG CHIAK YOT

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE (RADIOLOGY)

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MAY 2018

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ACKNOWLEDGEMENT

This thesis could never be completed without the assistance and attention to detail of many individuals who helped with the preparations of the thesis whose names may not all be enumerated. Those who were particularly helpful in the preparation of this thesis includes:

1. Dr. Nur Hartini Mohd Taib, medical physicist lecturer at Department of Radiology as the main supervisor of this dissertation. My most grateful appreciation is extended to Dr Nur Hartini, for her friendly guidance and patience with the tactful, constructive advice as the “polishing” process progressed.
2. Dr Juhara Haron, radiologist lecturer at Department of Radiology as my clinical supervisor for her persistent support and encouragement in the pursuit of completion of this thesis.
3. Associate Professor Dr Wan Ahmad Kamil, medical physicist lecturer who is my previous main supervisor of this dissertation. Without the guidance and encouragements from As. Professor Dr Wan Ahmad Kamil, this thesis would not be possible.
4. Dr Bilgins Keserci, Head of Clinical Science, MR Therapy Asia Pacific Region, Philips Healthcare.
5. Associate Professor Dr Mohd Shafie Abdullah, Associate Professor Dr Mohd Ezane Aziz, Dr Khairil Amir Sayuti, Dr Chandran, Dr Ahmad Tarmizi, Dr Wan Aireene and Dr Ahmad Hadif, the lecturers/radiologists all of whom directly or indirectly contributed their ideas and comments to the success of this study.

6. Dr Mohd Radhwan, a tactful and resourceful co-researcher and responsible and helpful colleague and friend.
7. Colleagues and all the staff in the Department of Radiology, HUSM.

I am greatly indebted to the many individuals who helped with the preparation of this thesis. Their contributions are sincerely appreciated and gratefully acknowledged.

TABLE OF CONTENTS

ACKNOWLEDGEMENT i

TABLE OF CONTENTS iii

LIST OF TABLES vi

LIST OF FIGURES vii

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS x

ABSTRAK 1

ABSTRACT 2

CHAPTER 1: BACKGROUND 4

1.1 Introduction 5

1.2 Objectives 8

1.2.1 General Objective: 8

1.2.2 Specific Objectives: 8

CHAPTER 2: LITERATURE REVIEW 9

2.1 MR-HIFU system: Concept of MR Thermometry 10

2.2 MR-HIFU system: Temperature Mapping 11

2.3 MR-HIFU System: Ablation system 12

2.4 Thermodynamics: Effects of Sonication Distance and Sonication Cell Size in affecting Near field Temperature changes. 13

2.5 Definition of Near Field 15

2.6 Experimental Ablation Targets: Phantom, Ex Vivo Porcine Tissue & Uterine fibroids 15

2.7	Applications of MR-HIFU	16
2.8	Complications of MR-HIFU	19
CHAPTER 3:	METHODOLOGY	22
3.1	Study Design	23
3.2	Methods and Materials	23
3.2.1	Phantom	23
3.2.2	MR HIFU system	24
3.2.3	MR HIFU Planning and Sonication	25
3.3	Variable Definitions (Outcome and independent variables)	29
3.4	Research Tools	30
3.5	Images Analysis and Interpretation	30
3.6	Statistical Analysis	31
3.7	Operational Definition	32
3.8	Ethical Consideration	33
CHAPTER 4:	MANUSCRIPT	34
ABSTRACT		37
INTRODUCTION		39
MATERIALS AND METHODS		42
RESULTS		50
DISCUSSION		52
CONCLUSION		56
ACKNOWLEDGEMENT		56
REFERENCES		57
CHAPTER 5 :	TABLES AND FIGURES	64
Tables		65

Figures 69

CHAPTER 6: REFERENCES 85

CHAPTER 7: APPENDICES 92

Appendix A : Flow chart for methodology 93

Appendix B : Ethical approval letter 94

Appendix C : Data collection sheet 95

Appendix D : Guidelines instructions to authors of selected journal 96

LIST OF TABLES

Table 1: Collected raw data from 125 sonication. 65

Table 2 Mean Temperature with sonication distance and sonication cell size 66

Table 3: Pearson product moment correlation test between sonication size and mean temperature changes. 66

Table 4: Regression model summary between sonication cell size and mean temperature changes. 66

Table 5: Coefficient table for regression equation to predict near field mean temperature changes with sonication cell size. 67

Table 6: Pearson product moment correlation test between sonication distance and mean temperature changes 67

Table 7: Regression table between sonication distance and mean temperature changes. 67

Table 8: Coefficient table for regression equation to predict near field mean temperature changes with sonication distance. 68

Table 9 Summary of simple linear regression analysis to determine factors associated with mean temperature changes in near field by ºC (n=25)................................... 68

LIST OF FIGURES

Figure 1: Comparison between an illustrated diagram and Monitor Stack B image demonstrating the near field as labelled in orange stripes on the left diagram. 69

Figure 2: Philips Sonavelle MR-HIFU quality assurance phantom provided by Philips was used during the study. 69

Figure 3: Shim box placement at 4cm using a measurement ruler on the MR console...... 70

Figure 4: Pre-treatment planning 3D fat suppressed T2-weighted images which was imaged using MRI and subsequently transferred to the HIFU console as monitoring stacks. 70

Figure 5: Planning Target Volume (PTV) view- The red coloured elliptical shaped region is assigned as PTV 71

Figure 6: Treatment cell setting within the previously assigned PTV- The smaller green circles are the treatment cells which was sonicated. 71

Figure 7: Philips Sonalleve MR-HIFU console during phantom ablation procedure,.... 72

Figure 8: Monitor stack A of coronal slice showing temperature map at target. 72

Figure 9: Monitor Stack B of sagittal slice showing temperature map at target. 73

Figure 10: Monitor Stack C of coronal slice showing temperature map at the near field. 73

Figure 11: Monitor Stack D of sagittal slice with temperature map on the far field. 74

Figure 12: Sonication using 2mm cell size, sonication distance 4cm away from transducer with sonication power 120W and intersonication cooling time of 60 seconds. 74

Figure 13: Sonication using 4mm cell size, sonication distance 4cm away from transducer with sonication power 120W and intersonication cooling time of 60 seconds. 75

Figure 14: Sonication using 8mm cell size, sonication distance 4cm away from transducer with sonication power 120W and intersonication cooling time of 60 seconds. 75

Figure 15: Pre-sonication using 12mm cell size, sonication distance 4cm away from transducer with sonication power of 120W and intersonication time of 60 seconds. 76

Figure 16: Post sonication using 12mm cell size, sonication distance 4cm away from transducer with sonication power of 120W and intersonication time of 60 seconds with temperature measurement taken in the pixel of interest. 76

Figure 17: Sonication using 16mm cell size, sonication distance 4cm away from transducer with sonication power 120W and intersonication cooling time of 60 seconds. 77

Figure 18: Crossed cursor used to select the Pixel of Interest (POI) for temperature measurement. 77

Figure 19: Real time time- temperature curve at the target cell. 78

Figure 20: Time-temperature curve post sonication. 78

Figure 21: Normality testing with P-P Plot for sonication cell size. 79

Figure 22: Normality testing with P-P Plot for sonication distance. 79

Figure 23: Histogram plotted for sonication cell size for normality testing.................. 80

Figure 24: Histogram plotted for sonication distance for normality testing.................. 80

Figure 25: Scatterplot for sonication cell size showing homoscedasticity..................... 81

Figure 26: Scatterplot for sonication distance for homoscedasticity............................. 81

Figure 27: Graph for repetition for 2mm cell size.. 82

Figure 28: Graph for repetition for 4mm cell size. 82

Figure 29: Graph for repetition for 8mm cell size 83

Figure 30: Graph for repetition for 12mm cell size. 83

Figure 31: Graph for repetition for 16mm cell size 84

Figure 32: Temperature variation for different sonication distance and cell size 84

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS

MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
MR-HIFU	Magnetic Resonance High Intensity Focused Ultrasound
POI	Pixel of Interest
ROI	Region of Interest
PRF	Proton Resonance Shift
WAFT-MRI	Water and Fat Separated Thermal Magnetic Resonance Imaging
tPA	Tissue Plasminogen Activator
QA	Quality Assurance
USM	Universiti Sains Malaysia
PMMA	PolyMethyl MetaAcrylate

ABSTRAK

Objektif: Tujuan kajian ini adalah untuk mengenal pasti korelasi di antara saiz sel sonikasi dan jarak sonikasi dengan perubahan purata suhu puncak pada kawasan medan dekat menggunakan "MR Thermometry" semasa MR-HIFU. Tujuan lain kajian ini adalah untuk merumuskan ramalan tindak balas terapi antara saiz sel sonikasi dan jarak sonikasi dengan perubahan purata suhu puncak pada kawasan medan dekat.

Metodologi: Jarak sonikasi dan saiz sel sonikasi telah ditetapkan secara berasingan. Sebanyak 125 sonikasi dilakukan. Bagi setiap parameter, purata suhu puncak telah diukur. Analisis univariat (korelasi Pearson) dan analisis multivariate (regresi linear) telah dilakukan untuk menentukan korelasi dan meramalkan tindak balas terapi. Tahap keertian telah dikira dengan $P < 0.05$ dinilaikan sebagai bererti.

Keputusan: Korelasi yang bererti antara saiz sel sonikasi dengan perubahan purata suhu puncak pada kawasan medan dekat, dengan nilai P kurang daripada 0.05. Namun, didapati tiada korelasi di antara jarak sonikasi dengan perubahan purata suhu puncak pada kawasan medan dekat, di mana nilai P adalah 0.08. Analisis regresi menyatakan bahawa saiz sel sonikasi menyangka perubahan suhu [$R2 = .654$, $F(1, 23) = 46.307$, $p < .001$]. Ramalan perubahan purata suhu mengikut saiz sel sonikasi iaitu 37.1 + .32 (saiz sel sonikasi) dalam milimeter ketika purata suhu diukur dalam darjah Celsius. Perubahan purata suhu dalam medan dekat meningkat 0.32 terhadap setiap milimeter saiz sel sonikasi.

Kesimpulan: Korelasi yang bererti didapati di antara saiz sel sonikasi dengan perubahan purata suhu dalam medan dekat. Walaubagaimanapun, tiada korelasi yang bererti didapati di antara jarak sonikasi dan perubahan purata suhu. Ujian regresi bagi saiz sel sonikasi telah menunjukkan regresi linear yang bererti antara saiz sel sonikasi dengan perubahan purata suhu puncak.

Kata kunci: Saiz sel sonikasi, jarak sonikasi, perubahan purata suhu

ABSTRACT

Objective: The purpose of this study is to determine correlation between sonication cell size and sonication distance with mean peak temperature changes within the near field and using MR thermometry during MR-HIFU. The other purpose of this study is to formulate a prediction of therapeutic response in between sonication cell size and sonication distance with mean peak temperature changes within the near field.

Methodology: Sonication distance and sonication cell size was controlled respectively, Total of 125 sonication was performed. For each 5 repetitions of sonication for a preset parameter, a mean peak temperature is measured. Univariate (Pearson correlation) and multivariate (linear regression) was performed to determine correlation and determine predictions of therapeutic response is done. The level of significance is calculated and the P value of less than 0.05 is statistically significant.

Results: There is statistically significant correlation between sonication cell size and mean peak temperature changes in the near field, with p value less than 0.05. However, no statistically significant correlation between sonication distance and mean peak temperature changes, with p value of 0.08. Regression analysis indicates that sonication cell size significantly predicted mean temperature changes in the near field. [$R2 = .654$, $F (1, 23) = 46.307$, $p < .001$]

Predicted mean temperature changes in the near field is equal to 37.1 + 0.32 (sonication cell size) in millimeters when the mean temperature is measured in Celsius. Mean temperature changes in the near field increased 0.32 with each millimeter of sonication cell size.

Conclusion: There is statistically significant correlation between sonication cell size and mean peak temperature changes in the near field however no statistically significant correlation between sonication distance and mean peak temperature changes.

Keywords: Sonication cell size, Sonication distance, Near field mean temperature changes.

CHAPTER 1 : BACKGROUND

1.1 Introduction

Magnetic Resonance High Intensity Focused Ultrasound (MR-HIFU), alongside many other noninvasive therapeutic intervention techniques has been introduced since the dawn of science as an alternative to adjunct surgical procedures in treating detectable lesions, particularly malignant lesions. MR-HIFU was one of the breakthroughs which uses a focused ultrasound beam to destroy detectable lesions, leaving surrounding tissues safe. Since its approval for therapeutic purposes in October 2004 by Food & Drug Administration (Diakite *et al.*, 2014; Ringold, 2004), it is commonly used to ablate prostatic tumours (Gelet *et al.*, 1999), uterine fibroids (Bohlmann *et al.*, 2014; Fruehauf *et al.*, 2008; Kim *et al.*, 2012b; Zhang *et al.*, 2010), breast carcinoma (Gianfelice *et al.*, 2003; McDannold *et al.*, 2007; Wu *et al.*, 2002), kidney (Illing *et al.*, 2005) and liver tumours (Illing *et al.*, 2005; Kennedy *et al.*, 2004; Keserci *et al.*, 2006; Li *et al.*, 2009; Zhang *et al.*, 2009). There have also been advancements for ablations of brain tumour as well (Jagannathan *et al.*, 2009).

MR-HIFU uses the concept of focusing high intensity ultrasound beam to a targeted point so that the targeted point accumulates energy and in turn raises the temperature. As the temperature of the targeted tissue increases, it burns the targeted tissue and causes tissue necrosis. Hence without surgical incisions the targeted tissue is destroyed and thus it is highly preferred by patients who refuses aggressive surgical interventions.

MR-HIFU is extensively used for uterine fibroid ablations in Department of Radiology Hospital University Sains Malaysia. During the procedure, each patient will be lying prone with the anterior abdomen lying in contact with the ultrasound transducer gapped by a acoustically homogenous diaphragm. As the ultrasound transducer is being activated to deliver high energy ultrasound beams, the Magnetic Resonance Imaging (MRI) is being utilized to monitor the tissue temperature. During the procedure, an MR sequence, specifically "MR temperature mapping" is used so the temperature of ablation can be monitored. Regular temperature measurement using thermometers is not feasible as most thermometers are not MRI compatible. The target temperature normally between 60 to 85 degrees as this the range when tissue necrosis occurs.

Although MR-HIFU is the future of interventional procedures, it still has its downfalls complications since it was first introduced. Among which the most common complication is pain and skin burns (Bohlmann *et al.*, 2014; Leon-Villapalos *et al.*, 2005; Leung *et al.*, 2014; Li *et al.*, 2007; Li *et al.*, 2009; R Hill *et al.*, 1994; Zhang *et al.*, 2009). Other complications are region of ablation dependant.

Near field region is defined as the volume through which the ultrasound beam transverses towards the treatment cell. In uterine fibroid treatments, the nearfield contains part of patient's abdomen, skin and subcutaneous tissue. Numerous reasons has been identified as causes of skin burns within the near field post MR-HIFU which consists of gaps in between acoustic coupling cushions, which can consist of folds (Fruehauf *et al.*, 2008) or air bubbles within the coupling ultrasound gel (Hacker *et al.*, 2006), poor skin preparation (Zhang *et al.*, 2010) and anterior abdominal defects which can consist of scar and dimple (Furusawa *et al.*, 2007). All these causes are attributed to heat accumulation within the near field.

Therefore, the aim of this study is to determine the effects of near-field temperature variations, in the form of temperature rise, in successive volumetric MR-HIFU sonication using phantom.

According to Kim *et al.* (2012b), it was reported that with reduction of the sonication distance and increment of the sonication cell size, the required energy consumption and time required for ablation has significantly improved.

There are no experimental studies studying on the effects of altering sonication cell size in affecting near field temperature variation. There is however an experimental phantom validation study using tissue mimicking phantom and ex vivo porcine muscle tissue, which was experimented by Hipp *et al.* (2012), which reports near field temperature changes is inversely proportional to sonication distance. However, no detailed near field temperature related analysis during successive sonication were performed.

1.2 Objectives

1.2.1 General Objective:

To study the effects of different sonication cell size and sonication distance on near field temperature variations using MR-HIFU phantom.

1.2.2 Specific Objectives:

i. To determine the correlation between sonication distance and sonication cell size with near field temperature variations using MR-HIFU phantom.

ii. To predict the near-field temperature variations with changes of sonication distance and sonication cell size using MR-HIFU phantom.

CHAPTER 2 : LITERATURE REVIEW

2.1 MR-HIFU system: Concept of MR Thermometry

According to Peek and Wu (2018), the MR-HIFU system consists of 3 main components which are the MR-HIFU table, the MRI unit and MR-HIFU console. However, the two most essential components in MR-HIFU system are the MR-HIFU table and the MRI scanner unit.

The importance of the MR-HIFU table is that it contains an ultrasound transducer which is embedded within the table. According to Rueff and Raman (2013), the ultrasound transducer delivers high intensity focused ultrasound to target tissue, resulting in tissue heating and subsequently cell death.

According to Diakite *et al.* (2014), the MRI temperature mapping system uses the HIFU console to constantly monitor the changes in temperature during sonication, which improves safety of the treatment. Temperature changes on the ablated tissue is measured based on the phase differences on two subsequent dynamic images.

$$\Delta T = \frac{\phi - \phi_0}{\alpha \gamma B_0 TE}$$

ΔT is the temperature change

$\phi - \phi_0$ is the phase difference in between 2 subsequent dynamic images.

B_0 is the magnetic field strength, 3T

α is 0.0094ppm/C

γ is 42.58

TE is echo time

2.2 MR-HIFU system: Temperature Mapping

Hindman (1966) published a study about the molecular forces and hydrogen bond formation between water molecules which produces chemical shift and gives rise to the proton resonance frequency (PRF) temperature sensitivity. Hindman's study gave way to MR spectrometry and was further adapted by Ishihara *et al.* (1995) in the development of MR temperature mapping.

According to Ishihara *et al.* (1995), instead of using spin echo pulse sequences to produce temperature dependence water proton chemical shifts, field echo pulse sequences are used. This improves acquisition time and improves temperature resolution.

According to Vigen *et al.* (2003), temperature mapping in MR-HIFU system has been utilizing PRF MR thermometry where two dynamic subsequent images are used to calculate the phase difference. It is relatively accurate as the temperature rises, it reduces the hydrogen ions resonant frequency and this in turn gives a reference-based proton resonant frequency MR thermometry.

According to Peters *et al.* (1998), PRF MR thermometry is accurate and it is independent of tissue type, at least for non-fatty tissue. However, according to Peters and Henkelman (2000), PRF thermometry is affected by changes in electrical conductivity of tissues. Besides, De Poorter (1995) suggested that PRF was flawed by its sensitivity to interscan motion. Hence modifications of techniques has been introduced since then, such as Water and Fat thermal (WAFT) MRI (Soher *et al.*, 2010) and 3D PRF T1 method as introduced by Diakite *et al.* (2014).

Nevertheless, in all the proposed methods of MR thermometry, fat only tissue poses the challenge in terms of measurement. Although most superficial tissue contains fractions of water, near field heat monitoring is lacking due to the fact there is no evidence substantiated method of fat only MR thermometry. This gives rise to complications occurring in the near field. It was proposed by Rieke and Pauly (2008) that in order to derive fat temperature mapping, fat suppression technique is used in T1, D or PRF methods. However, this only improved registration for displacement corrections in between scans.

Finally, Ragan and Bankson (2010) proposed 2-point Dixon technique is more superior to chemical saturation technique in fat suppression technique which is a cornerstone to introduction of fat temperature mapping in the future.

2.3 MR-HIFU System: Sonication system

According to Wijlemans *et al.* (2012), it was reported initially MR-HIFU was incorporating conventional point-by-point ablation technique, which is the entire target tissue being ablated sequentially by using multiple small foci of mini targets of millimetre in diameter. The disadvantage of this technique is that it was time consuming and not energy inefficient.

According to Salomir *et al.* (2000), it was reported "moving the focal point along double inside-out spiral trajectory covering the target region under continuous and maximal power for minimal treatment time". This spiral trajectory provides constant heat deposition in the centre of the target region and provides a larger area of ablation.

Hence with this theory, volumetric ablation technique was developed. According to Kim *et al.* (2012b), volumetric ablation technique was not only energy efficient but less time consuming. Voogt *et al.* (2012) also reported post volumetric MR-HIFU ablated uterine fibroid had a higher non-perfused volume, namely successful ablation and with no serious adverse effect reported.

2.4 Thermodynamics: Effects of Sonication Distance and Sonication Cell Size in affecting Near field Temperature changes.

According to Kaviany (2014), heat is atomic motion of matter in order to achieve equilibrium in atomic motion. Nonequilibrium state by a temperature gradient leads to heat transfer. Heat transfer physics describes thermodynamics and kinetics which involves energy storage, transport and transformation by means of principal energy carriers, which are energy containing particles.

According to Dhenin and Ernsting (1978), there are 3 main methods of heat transportation, which are conduction, convection and radiation. Conduction is a process of heat transfer where the heat is exchanged between objects at different temperature in contact with each another. Convection is a process "when a fluid (liquid or gas) at one temperature flows over a surface at a different temperature, heat is gained or lost by convection”. Radiation is a process of heat transfer utilising electromagnetic waves spreading out from the heat origin.

According to Shen *et al.* (2005), the mechanism of heat transfer within the human body has been postulated using Pennes bioheat transfer equation. Pennes bioheat equation was able to predict thermal storage, conduction and generation despite presence of energy exchange between blood vessels and surrounding tissue.
Hence despite newer bioheat transfer theories has been introduced after that, Pennes bioheat transfer equation still remains closest taken into consideration when it comes to deciding temperature related safety of a medical ablation device.

According to Mougenot *et al.* (2009), near field cumulative heating induced during successive MR-HIFU ablation is proven and attributed to by transducer displacement and baseline drift correction. However, quantification of the susceptibility changes due to these factors are still currently being investigated as quantification of susceptibility changes enables cumulative heating monitoring.

According to Kim *et al.* (2012b), it was reported that with reduction of the sonication distance and increment of the sonication cell size, the required energy consumption and time required for ablation has significantly improved. There were reported minor complications in the study populations however it was not elaborated during which sonication distance or using which sonication cell size due to the subjects being categorised within the exclusion criteria.

2.5 Definition of Near Field

According to Philips Medical Systems MR-HIFU Fibroid Therapy System Instruction Manual (2010), near field is defined as the volume through which the ultrasound beam transverses towards the treatment cell. In uterine fibroid treatments, the nearfield contains part of patient's abdomen, skin and subcutaneous tissue.

In a study conducted among population in United Kingdom, the average thickness of subcutaenous fat measured on MRI image was found in range of 2.3 ± 0.8 cm (De Lucia Rolfe *et al.*, 2010). While in another study performed on female Turkey population, the average thickness found was 1.79 ± 0.9 cm (Akkus, 2012).

Bour *et al.* (2017) reported that with the monitoring stacks as safety mechanism of the system to monitor temperature so as if the temperature rises to beyond safety limits, warning alarm will be triggered. These zones are called warning zones.

2.6 Experimental Sonication Targets: Phantom, Ex Vivo Porcine Tissue & Uterine fibroids

Phantoms has been used for quality control and assurance in literally all imaging devices from fluoroscopic units, computed tomography (CT) and MRI as well. The purpose of quality assurance is to maintain imaging quality and prevent complications which can be due to equipment malfunction. (Hipp *et al.*, 2012). Beside by that, quality assurance phantom should be structurally and compositionally uniform and homogenous, according to Partanen *et al.* (2009), to improve reliability. According to

King *et al.* (2007), phantoms should be thermally and acoustically similar to soft tissue.

According to Partanen *et al.* (2009), phantom material of composition with 2-3% mass concentration of agar silica adequately mimics soft tissue with following physical properties: ultrasound attenuation coefficient = 0.58 ± 0.06 dB/cm (@1MHz) , ultrasound speed = 1490 ± 10 m/s, density = 1.03 ± 0.01 g/cm^3 , acoustic impedance = 1.54 ± 0.01 x 106 kg/(m^{2}s).

According to Hipp *et al.* (2012), tissue mimicking phantom and ex vivo porcine tissue were used in an experimental study using phantom and ex vivo porcine muscle tissue during single sonication through different interfaces which are acrylic, rubber and air. Temperature changes are measured during the experiment using MR temperature mapping and direct temperature measurement.

Mougenot *et al.* (2009) reported that cumulative heating in successive ablation using an 80 kg pig as a target in accordance with French laws governing the care and the use of animals for research.

2.7 Applications of MR-HIFU

MR-HIFU uses high intensity frequency ultrasound to ablate targeted tissues using the concept of thermal ablation. Thermal ablation refers to tissue destruction by subjecting the targeted tissue with extremes of temperature which can be divided to hyperthermic thermal ablation and hypothermic thermal ablation(Brace, 2011).

Since FDA approval of MR-HIFU for uterine fibroid treatment (Bohlmann *et al.*, 2014; Fruehauf *et al.*, 2008; Kim *et al.*, 2012b; Zhang *et al.*, 2010) in year 2000 (Ringold, 2004), it has been widely used for various tissue ablations.

Uterine fibroid MR-HIFU ablation is the most widely recognized application. An early exploration of applications of MR-HIFU in context of treatment of uterine fibroid was promising with 79.3% of patients treated with MR-HIFU significantly reduced in symptoms with uterine fibroid size mean reduction of 13.5% (Hindley *et al.*, 2004). Multiple other subsequent studies with favorable results are being published. (Bohlmann *et al.*, 2014; Fruehauf *et al.*, 2008; Kim *et al.*, 2012b; Zhang *et al.*, 2010).

Other widely used applications to MR-HIFU are on breast carcinoma (Gianfelice *et al.*, 2003; McDannold *et al.*, 2007; Wu *et al.*, 2002), hepatoma (Illing *et al.*, 2005; Kennedy *et al.*, 2004; Keserci *et al.*, 2006; Li *et al.*, 2009; Zhang *et al.*, 2009), prostate carcinoma (Gelet *et al.*, 1999), renal cell carcinoma (Illing *et al.*, 2005).

Hepatocellular carcinoma has been identified as the most common primary malignancy of liver and 5th most common malignancy worldwide (Jemal *et al.*, 2011). According to Willatt *et al.* (2008), as the incidence of alcoholism and hepatitis B is on the rise, it is expected hepatocellular carcinoma to increase in incidence. Besides by that liver metastasis is also on the rise as the incidence of common primary malignancies like colon, breast, lung and stomach carcinoma are on the rise.(Sica *et al.*, 2000). According to Kim *et al.* (2012a), combination therapy of MR-HIFU ablation and transarterial chemoembolism(TACE) is more effective than TACE monotherapy. Another study conducted by Khokhlova *et al.* (2015) highlights the usage of chemotherapeutic drugs within microbubbles which are introduced intravenously and with MR-HIFU sonicating the target lesions causing destruction of microbubbles, in turn releasing chemotherapeutic drugs into the tumour directly.

Another notorious gastrointestinal malignancy for its insidious onset is pancreatic carcinoma. With the help of MR-HIFU, incorporating the similar application using MR-HIFU enhancing chemotherapeutic drug microbubble release as seen in MR-HIFU treatment for hepatoma, results has been promising in small scale studies which are yet to be proven in large scale clinical trials (Khokhlova *et al.*, 2015).

Recent newly introduced applications are thyroid cancer ablation, which was mentioned by Lang *et al.* (2017) comparing open thyroidectomy and MR-HIFU ablation on malignant thyroid nodules with higher efficacy and shorter hospital stay in the latter.

Other promising areas of application of MR-HIFU was hemorrhagic control. According to Zderic *et al.* (2006), animal studies has been conducted with MR-HIFU treatment applied on punctured arteries in 15 animals and all 15 animals showed hemostasis with no immediate or delayed complications. Another study done by Hynynen *et al.* (1996) on animal studies also show promising results in MR-HIFU arterial occlusion.

According to Stone *et al.* (2007), clot lysis can utilize the application of MR-HIFU mediated therapy as an adjunct with thrombolytic treatment. This is particularly useful in treating patients with ischemic stroke. A pilot study was conducted comparing tissue plasminogen activator (tPA) mediated thrombolysis alone and MR-HIFU mediated tPA thrombolysis and it showed complete recanalization of thrombosed blood vessels in combination therapy in comparison with partial recanalization of thrombosed blood vessel in standalone tPA thrombolytic treatment.

Non-MRI based HIFU has an aesthetic role to play. This application does not require MRI monitoring as HIFU was used to treat wrinkles and skin laxity. According to Park *et al.* (2015), it was reported that ultrasound transducer is applied directly on sagging and wrinkled skin and provides tightening and smoothening effects. Thus, HIFU is a noninvasive safe and effective procedure to reduce wrinkles and sagging skin.

2.8 Complications of MR-HIFU

Although MR-HIFU is the future of interventional procedures, it still has its downfalls complications since it was first introduced. Among which the most common complication is pain and skin burns (Bohlmann *et al.*, 2014; Leon-Villapalos *et al.*, 2005; Leung *et al.*, 2014; Li *et al.*, 2007; Li *et al.*, 2009; R Hill *et al.*, 1994; Zhang *et al.*, 2009). Other complications are region of ablation dependant.

Pain is the most common complication reported in all MR-HIFU procedures regardless of region (Deckers *et al.*, 2015; Kim *et al.*, 2015; Leung *et al.*, 2014;

Wang *et al.*, 2012; Wu *et al.*, 2002; Zhang *et al.*, 2013). The subcutaneous layer is interspersed with nerve endings in the whole subcutaneous layer with the richest of all later in between epidermis and dermis layer (Ng and Lau, 2015). As the ultrasound pathway decay occurs along the beam pathway, both thermal energy and mechanical energy generated by the ultrasound is detected by the sensitive nerve endings, which causes pain.

Skin burn is the 2nd most common complication after pain. According to Kagan *et al.* (2013), classification of skin burns can be divided into 3 degrees depending on the depth of involvement. 1st degree burns involves epidermis, 2nd degree burns involve dermis layer and 3rd degree involves the epidermis, dermis and often involves subcutaneous fat as well. As high intensity ultrasound is used for thermal ablation, concerns of beam path damages has raised awareness among researchers that near field thermometry is essential to prevent complication. Although the incidence of complications in the near field is not alarming, with only one reported full thickness skin burn requiring surgery (Leon-Villapalos *et al.*, 2005) while superficial skin burns are not uncommon in practice. According to Li *et al.* (2009), incidence of superficial burn involving grade 1 and 2 burns during liver tumour ablation are common where all the 59 patients with hepatocellular carcinoma who undergone MR-HIFU, all of which sustain certain degree of skin burn with 48 patients (67%) sustain second degree skin burn. While 8 patients (14%) sustained 1st degree burn and 3 patients (5%) sustained 3rd degree burns.

Skin burns are common in patients with skin scars, with the therapeutic ultrasound beam deposits its energy as it transverses the abdominal scar. According to Zhu *et al.*

(2016), applications of scar patch on the abdominal scar was advised to prevent skin burns.

Numerous reasons has been identified as causes of skin burns post MR-HIFU which consists of gaps in between acoustic coupling cushions, which can consist of folds (Fruehauf *et al.*, 2008) or air bubbles within the coupling ultrasound gel (Hacker *et al.*, 2006), poor skin preparation (Zhang *et al.*, 2010) and anterior abdominal defects which can consist of scar and dimple (Furusawa *et al.*, 2007).

CHAPTER 3: METHODOLOGY

3.1 Study Design

This is an experimental study using phantom which was conducted in Department of Radiology, Hospital Universiti Sains Malaysia Hospital (HUSM), Kubang Kerian, Kelantan from July 2015 until April 2018.

3.2 Methods and Materials

3.2.1 Phantom

Throughout the study only one quality assurance sonication phantom was used for sonication.

Quality Assurance (QA) Sonication phantom (Philips Medical Systems, Ayrintie 4, Vantaa, Finland) with serial number: E-1929-4 was used for ablation. Dimension of the phantom measures 19cm in diameter and 19cm in height with volume of $5388cm^3$. (Figure 2). Acoustic properties of the phantom are of which the ultrasound speed is 1536 m/sec and attenuation is 0.417 dB/ cm MHz, density is 1.03 g/cm^3 and acoustic impedance is 1.54 x 106 $kg/(m^2s)$

According to QA sonication phantom manual provided by Philips Medical Systems (2005), The quality assurance sonication phantom is a polymethyl metacrylate (PMMA) container filled with a polymer mixture containing mainly gel. After filling, the polymeric mixture inside the phantom becomes solid and cannot be removed from the container.

3.2.2 MR HIFU system

Experiments was conducted using an integrated clinical MR-HIFU system (Sonalleve, Philips Medical Systems, Vantaa, Finland and Philips Achieva TX 3 Tesla, Philips Healthcare, Best, the Netherlands) had a phased arrayed 256 channel ultrasound transducer which is composed of an aperture diameter of 12.8cm, radius of curvature of 12cm and a focal length of 12cm. The emitted ultrasound was at 1.2MHz. The transducer was equipped with a mechanical displacement device with 5 degrees of freedom (three translational and two rotational). This system was able to perform volumetric ablation with or without binary feedback control. The system provided 5 different sized ellipsoidal treatment cells that were 2mm, 4mm, 8mm, 12mm and 16mm in axial dimension and 10 mm, 20 mm, 30mm or 40mm in longitudinal dimension, respectively.

MR images for treatment planning were acquired using 3D T2-weighted turbo spin echo (TSE) pulse sequence [TR/TE = 1000 / 130ms, echo train length = 62, field of view (FOV) = 250 x 250 x 122 mm, acquisition matrix = 160 x 111 x 90, reconstructed in plane voxel size = 0.49mm, number of averages = 2]. Dynamic temperature monitoring based on changes in proton resonance frequency (PRF) was performed using 2D fast field echo (FFE) segmented echo-planar imaging (EPI) [TR/ TE = 38 /20 ms, flip angle = 19.5º, EPI factor = 11, FOV = 200 x 200mm, acquisition matrix =100 x 100, slice thickness = 7mm, number of slices = 6, in plane pixel size = 1.25mm]